US009408911B2

(12) **United States Patent**
Ryu et al.

(10) **Patent No.: US 9,408,911 B2**
(45) **Date of Patent: Aug. 9, 2016**

(54) **ANTICANCER PRODRUGS ACTIVATED BY RADIATION OR ULTRAVIOLET TREATMENT AND USE THEREOF**

(71) Applicant: **Korea Institute of Science and Technology**, Seoul (KR)

(72) Inventors: **Ju-Hee Ryu**, Seoul (KR); **Kwang-Meyung Kim**, Seoul (KR); **Ick-Chan Kwon**, Seoul (KR); **Kui-Won Choi**, Seoul (KR); **Sang-Yoon Kim**, Seoul (KR); **Beom-Suk Lee**, Seoul (KR); **Dae-Yoon Chi**, Seoul (KR); **Hee-Seup Kil**, Seoul (KR); **Hyun-Ju Sung**, Seoul (KR)

(73) Assignee: **KOREA INSTITUTE OF SCIENCE AND TECHNOLOGY**, Seoul (KR)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **14/974,490**

(22) Filed: **Dec. 18, 2015**

(65) **Prior Publication Data**

US 2016/0184430 A1 Jun. 30, 2016

Related U.S. Application Data

(62) Division of application No. 14/001,745, filed as application No. PCT/KR2011/001438 on Mar. 2, 2011.

(51) **Int. Cl.**

A61K 41/00	(2006.01)
A61N 5/06	(2006.01)
A61N 5/10	(2006.01)

(52) **U.S. Cl.**

CPC ***A61K 41/0042*** (2013.01); ***A61N 5/1001*** (2013.01)

(58) **Field of Classification Search**

None

See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

2004/0052793	A1	3/2004	Carter et al.
2007/0104719	A1	5/2007	Carter et al.
2008/0193431	A1	8/2008	Zheng et al.
2013/0338422	A1	12/2013	Ryu et al.

OTHER PUBLICATIONS

Kim, "Development of a prodrug activated by caspase-3," www.riss.kr/link?id=T11929818, uploaded Feb. 2010, Abstract.

Law, Benedict et al. "Proteolysis: A Biological Process Adapted in Drug Delivery, Therapy, and Imaging." Bioconjugate Chemistry vol. 20, No. 9, Sep. 2009, pp. 1683-1695.

Stefflova, Klara et al. "Targeted Photodynamic Therapy Agent with a Built-In Apoptosis Sensor for In Vivo Near-Infrared Imaging of Tumor Apoptosis Triggered by Its Photosensitization In Situ." Molecular imaging vol. 5, No. 4, 2006, pp. 520-532.

Rai, Prakash, et al. "Development and applications of photo-triggered theranostic agents." Advanced Drug Delivery Rreviews vol. 62, 2010, pp. 1094-1124.

Wojtyk, James TC, et al. "Exploiting tumour biology to develop novel drug delivery strategies for PDT." Medical Laser Application, vol. 21, 2006, pp. 225-238.

Kim, Sungwon, et al. "Engineered polymers for advanced drug delivery." European Journal of Pharmaceutics and Biopharmaceutics vol. 71, 2009, pp. 420-430.

Tamm, Ingo, et al. "IAP-Family Protein Survivin Inhibits Caspase Activity and Apoptosis Induced by Fas (CD95), Bax, Caspases, and Anticancer Drugs." Cancer Research, vol. 58, 1998, pp. 5315-5320.

International Search Report mailed Dec. 21, 2011 in corresponding International Application No. PCT/KR2011/001438.

Office Action issued on May 23, 2014 in U.S. Appl. No. 14/001,745 (US2013/0338422).

Office Action issued on Dec. 19, 2014 in U.S. Appl. No. 14/001,745 (US2013/0338422).

Notice of Allowance issued on Mar. 30, 2015 in U.S. Appl. No. 14/001,745 (US 2013/0338422).

Office Action issued on Sep. 28, 2015 in U.S. Appl. No. 14/001,745 (US2013/0338422).

Primary Examiner — Amber D Steele
Assistant Examiner — Schuyler Milton
(74) *Attorney, Agent, or Firm* — Foley & Lardner LLP

(57) **ABSTRACT**

The present invention relates to an anticancer prodrug consisting of peptide of acetyl-SEQ ID NO: 1-linker-anticancer drug. The anticancer prodrug effectively provides an anticancer drug unstable in acid and base, such as doxorubicin, in a form of prodrug. Thus, the anticancer prodrug exists as a non-toxic inactive form when administered into the body, but effectively releases the anticancer drug as an active ingredient in the target area in the presence of caspase activated by radiation or UV treatment after administered into the body. Accordingly, the anticancer drug exhibits selective anticancer effects on cancer cells, thereby maximizing the therapeutic effect and minimizing the side-effects of chemotherapy.

9 Claims, 27 Drawing Sheets